Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-19 (canceled)

Claim 20 (withdrawn): A pharmaceutical composition comprising a conformational variant obtained by the method of claim 1.

Claim 21 (withdrawn): A pharmaceutical composition according to claim 20, wherein the conformational variant is a protein antigen that binds to a neutralizing antibody with a higher affinity than a non-neutralizing antibody.

Claim 22 (withdrawn): A pharmaceutical composition according to claim 20, wherein the structure of the conformational variants is stabilized.

Claim 23 (withdrawn): A pharmaceutical composition according to claim 1, wherein the conformational variant protein antigen is capable of partially clearing or clearing neutralizing activity in serum in vitro.

Claim 24 (withdrawn): The pharmaceutical composition of claim 20, further comprising a microparticle.

Claim 25 (withdrawn): A pharmaceutical composition according to claim 24, wherein:

(a) said microparticle comprises a core comprising at least one protein molecule that comprises the same primary amino acid sequence as the protein antigen;

(b) said microparticle comprises a protein core composed of at least one protein molecule having greater than 95% amino acid sequence identity as the protein antigen;

(c) the protein core of (a) is surrounded by a pharmaceutically acceptable coating agent, that is releasable in vivo;

(d) said coating agent of (c) is selected from the group consisting of a biodegradable polymer, calcium phosphate, cellobiose and polyethylene glycol;

(e) said biodegradable polymer of (d) is selected from the group consisting of a polylactide, a polyglycolide, a poly(lactide-co-glycolide), poly (D,L-lactide-polyethylene glycol), a poly(sulphobutyl-polyvinylalcohol)-g-(lactide-co-glycolide), a polyhydroxybutyric acid, a polycaprolactone, a polyothoester, a polyanhydride, a polyesteramide, a polyamino acid, a polycyanoacrylate, a polyamide, a polyacetal, a polyetherester, a polydioxanone, a polyalkene alkylate and a biodegradable polyurethane;

(f) the microparticle comprises a pharmaceutically acceptable biodegradable polymer;

(g) said biodegradable polymer of (f) is selected from the group consisting of a polylactide, a polyglycolide, a poly(lactide-co-glycolide), poly (D,L-lactide-polyethylene glycol), a poly(sulphobutyl-polyvinylalcohol)-g-(lactide-co-glycolide), a polyhydroxybutyric acid, a polycaprolactone, a polyothoester, a polyanhydride, a polyesteramide, a polyamino acid, a polycyanoacrylate, a polyamide, a polyacetal, a polyetherester, a polydioxanone, a polyalkene alkylate and a biodegradable polyurethane;

(h) the microparticle comprises a metal salt;

(i) said metal salt of (h) is calcium hydroxide or aluminium hydroxide;

(j) the protein antigen is covalently bound to the surface of the microparticle.

Claim 26 (withdrawn): A pharmaceutical composition according to claim 20, wherein said composition further comprises an immunostimulatory molecule.

Claim 27 (withdrawn): A pharmaceutical composition according to claim 26, wherein said immunostimulatory molecule is a molecule that results in an elevated humoral response.

Claim 28 (withdrawn): A pharmaceutical composition according to claim 27, wherein said immunostimulatory molecule is IL-4, IL-5, IL-10 and IL-13.

Claim 29 (withdrawn): A pharmaceutical composition according to claim 20:

(a) suitable for causing an immune response in for immunization of a subject against a pathogen;

(b) which further comprises a second protein antigen;

(c) which further comprises an adjuvant; or

(d) suitable for partially or fully immunizing a subject against a pathogen from which the conformational variant was derived.

Claim 30 (withdrawn): The pharmaceutical composition of claim 29, wherein said pathogen is a:

(a) virus;

(b) bacteria; or

(c) fungus.

Claim 31 (new): A method of producing new conformational variants comprising the steps of:

providing a target protein to a multiwell plate;

denaturing said target protein under at least two denaturing conditions selected from the list consisting of: treating said target protein with organic solvents, treating said target protein with pH modifiers, treating said target protein with ionic detergents, and exposure of said target protein to sonication;

refolding said target protein to create conformational variants by varying at least two different conditions under which said target protein refolds wherein said conditions are selected from the list consisting of temperature, selection of buffer, and time of incubation;

stabilizing said conformational variants by cross linking with one or more cross linking agents;

testing said conformational variants by determining the affinity of said conformation variants for a panel of know antibodies, where at least one of said antibodies is a neutralizing antibody and at least one of said antibodies is a non-neutralizing antibody;

sorting said conformational variants based on the affinity of each conformation variant for said panel of know antibodies; and

selecting high affinity conformational variants for ability to clear neutralizing antibodies from the sera of infected individuals in vitro;

wherein said conformational variants have the same sequence of amino acids but differ in tertiary structure

Claim 32 (new): The method of claim 31, wherein said sorting of said conformational variants is done with a computer.